UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,377	09/15/2003	Yanbin Liang	17565 (AP)	2517

51957 7590 06/01/2006

ALLERGAN, INC., LEGAL DEPARTMENT
2525 DUPONT DRIVE, T2-7H
IRVINE, CA 92612-1599

EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,377	LIANG ET AL.	
	Examiner	Art Unit	
	Iqbal Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-56 and 61-66* is/are pending in the application.

4a) Of the above claim(s) *1-3,5,6 and 8-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 and 61-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is an US application filed on 9/15/2003.

The preliminary amendment filed on 3/8/2006 amending claim 5, canceling claims 4, and 57-60 and adding new claims 61-66 is acknowledged. Claims 1-3, 5-56 and 61-66 are at issue and are present for examination.

Applicant's election with traverse of Group I, Claims 7 and 61-66, drawn to a polynucleotide encoding COX-1 variant polypeptide and a protein of SEQ ID NO: 2 or nucleic acid encoding SEQ ID NO: 2 and peptide sequence of SEQ ID NO: 14 in the response filed on 3/8/2006 is acknowledged.

The traversal is on the ground(s) that there would be no burden of search for the coexamination of all the groups I-III simultaneously. This is not found persuasive because while the search necessary for examination of all the groups overlaps it is not coextensive, examination of Group I-III, would require search of subclasses unnecessary for the search of Group I, for example 435/189 and 530/387.9. As restriction is clearly permissible even among related inventions as defined in MPEP 808 and 35 U.S.C. 121 allows restriction of inventions, which are independent or distinct.

Applicants further argue that all the claims of Group I-III are closely related by polynucleotide, which is not persuasive as restriction is clearly permissible even among related inventions as defined in MPEP 808.

Applicants further argues about search of six sequences i.e. SEQ ID NOS: 1, 2, 7, 8, 14 and 16 on the basis that the MPEP 803.04 and stating that it would not impose any serious

burden on the Office and all the sequences should be examined together. Applicants traversal is not found persuasive for the following reasons:

Applicant is reminded that the MPEP recites **up to 10** distinct nucleotide sequences, and while applicants assert that they are claiming 6 independent and distinct sequences, they are in fact claiming many more than 6 independent and distinct sequences when one considers they are claiming each of SEQ ID NOs: 1, 2, 7, 8, 14 and 16 as well as corresponding nucleotide sequences and a search for each of the sequences would not be done solely by searching electronic sequence databases as such databases seldom provide extensive coverage of all variants which are known or have been made of a single protein such that word searching for each variant is required. Such searching would likely be different for each variant as each change may have distinct effects. Furthermore, even sequence searching of the six different variants would be a substantial burden on the office as each sequence has to be examined individually to determine if it includes each claimed variant and reference teaching one such variant would neither anticipate nor make obvious any of the other five. As such the novelty and non-obviousness of each variant would have to be addressed individually creating a large burden on the office.

"*For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP 808.02.*" (see MPEP 803).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-3, 5-6, and 8-56 are withdrawn from further consideration pursuant to 37 CFR

1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in communication filed on 3/8/2006.

Claims 7 and 61-66 are under consideration and are being examined herein.

Claim Objections

Claim 7 is objected to as depending from non-elected claims. Appropriate correction is required.

Claims 7 and 61-66 are objected to as encompassing non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 7 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 7 recites a "cell" which encompasses a natural cell. A natural cell is non-statutory subject matter. This rejection can be over come by stating "an isolated host cell"

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 7 (depends on claim 1) is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the present instance, claim 1 recites the "conservative variant thereof" which is unclear as to the scope of variants that are encompassed. What does the term "conservative" mean? While some changes (such as substitution of Lys for Arg) are clearly within the scope of this term, in the art the metes and bounds the term is not clear. For example in some situations replacement of Glu with Gln can be considered conservative in others it is not. Many other examples could be given. Furthermore, how many changes can be made to a polypeptide and still be a "variant thereof"?

Claim 7 (depends on claim 1) is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the present instance, claim 1 recites the "exogenously expressed polypeptide" which lacks antecedent basis in all of claims 1, 2 and 3. Also what does exogenously expressed mean?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 7 is directed to any cell comprising a DNA molecule ~~comprising a~~ encoding any comprising polypeptide ~~of~~ SEQ ID NO: 14. or any conservative variant thereof.

The specification does not contain any disclosure of the function of all peptide sequences comprising SEQ ID NO: 14 or any conservative variants thereof. The genus of cDNA that encodes the above peptide molecule is a large variable genus with the potentiality of encoding many different peptides. Therefore, many functionally unrelated peptides are encompassed within the scope of the claim. The specification discloses only several peptide species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a cell comprising a DNA molecule of SEQ ID NO: 1 encoding the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for any cell comprising any peptide sequence of seven amino acid residues comprising SEQ ID NO: 14 or any conservative variants of the peptide comprising SEQ ID NO: 14 having any function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 7 is so broad as to encompass any cell comprising any peptide sequence of seven amino acid residues comprising SEQ ID NO: 14 or any conservative variants of the peptide comprising SEQ ID NO: 14 having any function. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of peptides having no function broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to amino acid sequence of only several peptides.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions.

The specification does not support the broad scope of the claim which encompasses any cell comprising any peptide sequence of seven amino acid residues comprising SEQ ID NO: 14 or any conservative variants of the peptide comprising SEQ ID NO: 14 having any function because the specification does **not** establish: (A) regions of the peptide structure which may be

modified without effecting the peptide activity; (B) the general tolerance of peptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any peptide residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any cell comprising any peptide sequence of seven amino acid residues comprising SEQ ID NO: 14 or any conservative variants of the peptide comprising SEQ ID NO: 14 having any function. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any peptide having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 65-66 and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated host cells transformed with the recited nucleic acids does not reasonably provide enablement for host cells within a multicellular organism which have been transformed with the recited nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 65-66 and 7 are so broad as to encompass host cells transformed with specific nucleic acids, including cell in *in vitro* culture as well as cells within any multicellular organism. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of host cell broadly encompassed by the claims. While methods for transforming cell *in vitro* are well known in the art, methods for successfully transforming cells within complex multicellular organisms are not routine and are highly unpredictable. Furthermore, methods for producing a successfully transformed cell within one multicellular organism are unlikely to be applicable to transformation of other types of multicellular organisms as multicellular organisms vary widely. However, in this case the disclosure is limited to only host cell in vitro.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the use of host cells within a multicellular organism for the production of polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, expression of genes in a particular host cell having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is suggested that applicants limit the claims to "An isolated host cell".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 7 is rejected under 35 U.S.C. 102(e) as being anticipated by Kovalic et al. (US Pre-Grant Publication 20040172684, published 1/29/2004, claimed priority of US Application 09/850,147 filed on 5/8/2001). Kovalic et al. disclose the sequence of a protein (SEQ ID NO: 14452) of 153 amino acids, wherein amino acid number from 45-51 is 100% identical to SEQ ID NO: 14 of the instant application. Kovalic et al. also teach cloning the gene encoding the polypeptide and transformed a host cell with the nucleic acid and produced the polypeptide. Therefore, Kovalic et al. anticipate claims 7 of instant application.

Allowable Subject Matter

Claims 61 and 64 are allowable over prior arts of record.

Claims 65-66 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112 1st and 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

Status of the claims:

Claims 7 and 61-66 are pending.

Claims 7 and 65-66 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Iqbal Chowdhury, PhD, Patent Examiner
Art Unit 1652 (Recombinant Enzymes)
US Patent and Trademark Office
Rm. REM 2B69, Mail Box. 2C70
Ph. (571)-272-8137, Fax. (571)-273-8137
IC

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1652